

tions. But these cases of permanent albuminuria must not be confounded with those in which the albuminuria is transient. Here the prognosis is good, and as soon as the albuminuria disappears and stays away for a reasonable length of time we can regard such a case as healthy as if he had had simply an attack of functional dyspepsia.

It has been suggested that all cases of albuminuria could be insured by charging them all an extra premium, which could be so equalized that no loss would accrue to the company. This is undoubtedly true; but think how manifestly unjust it would be to the cases of transient albuminuria, who would thus be forced to pay extra, when in a few months or even weeks they might be considered in such good health as to be charged only the regular rates. It would be like accepting all cases of cough at an extra premium—a splendid opportunity for consumptives and cases of emphysema, but very harsh treatment for ordinary colds and acute bronchitis.

AMÆBIC DYSENTERY.¹

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SINCE the announcement of the discovery of the amœbæ coli in the United States by Osler, quickly followed by confirmatory reports from various sources of the presence of these organisms in the fecal discharges in cases of chronic dysentery, the subject of amœbic dysentery has assumed considerable importance. Lambl² was the first observer who noted the occurrence of rhizopods as human parasites, but his descriptions of the organisms which he observed show beyond doubt that they differ in many essential particulars from the one subsequently described by Loesch³ and others. He found amœboid bodies and other members of the above group in the mucus from the bowel of a child dead of enteritis in 1859. Following this studies were made by Loesch, who found amœbæ in the stools in a case of ulcerative inflammation of the colon. This case, which was in every way a typical one, originated in St. Petersburg. He produced the disease in a dog by rectal injections of the fresh stools from this case. Kartulis,⁴ in Egypt, found amœbæ present in the stools of over 500 cases of both acute and chronic dysen-

¹ Read by invitation before the Nashville Academy of Medicine.

² Lambl: Beobacht. u. Stud. aus den Franz-Josef-Kinder-Spital, 1860.

³ Loesch: "Massenhafte Entwicklung von Amœben in Dickdarm." Virch. Arch., Bd. lxx.

⁴ Kartulis: "Zur Aetiologie der Dysenterie in Aegypten." Virchow's Archiv, 1885, Bd. cv.; "Ueber tropische Leberabscesse und ihr Verhältniss zur Dysenterie." Virchow's Archiv, 1889, Bd. cxviii.; "Zur Aetiologie der Leberabscesse. Lebende Dysenterie Amœben im Eiter der dysenterischen Leberabscesse." Centralblatt f. Bakteriologie, 1887, Bd. xi.; "Ueber weitere Verbreitungsgebiete der Dysenterie Amœben." Centralblatt für Bakteriologie, 1890, Bd. vii.

tery. In twelve post-mortems the amœbæ were present in the ulcers in every case. He further studied microscopically the contents of twenty-two liver-abscesses, and found amœbæ present in all. Later he reports two cases originating in Athens. He also produced the disease in dogs and cats by rectal injections of the stools and both pure and contaminated cultures of the amœbæ. Massiutin¹ has, at Kiev, studied the question under Loesch's supervision. He found amœbæ, resembling in every particular those described by Kartulis, in the stools of five patients: one a case of chronic dysentery of several years' standing; the second, a man with chronic intestinal catarrh; a third, a case of typhoid fever with late diarrhœa and much mucus in the stools; the fourth and fifth were cases of diarrhœa with fluid, mucoid stools. He doubts their connection with the intestinal lesions. Hlava² found amœbæ in sixty cases of dysentery at Prague. He produced the disease in both cats and dogs by injecting stools containing amœbæ. Cases were also reported by Cahen,³ of Graz, and Nasse,⁴ of Berlin. Osler⁵ was the first to describe the amœbæ coli in this country. He found amœbæ present in the pus of a liver-abscess complicating chronic dysentery; the amœbæ were also found in the stools. The patient, who was a physician, contracted the disease while a resident in Panama some years before. Quickly following Osler's paper reports of cases of this disease came from various parts of this country. Stengel⁶ claimed to have found amœbæ in three cases of acute dysentery in Philadelphia, and a short time after Musser⁷ reported four cases from the same city. Rhein,⁸ also of Philadelphia, mentions that he found amœbæ in fifteen cases of dysentery, but gave no details. Dock⁹ was the first to find amœbic dysentery in the South, he having reported twelve cases of both acute and chronic forms of this disease occurring in and about Galveston. In a letter, Dr. Dock informs me that before leaving Texas he saw five more cases, but has searched in vain for amœbæ at his present location in Ann Arbor, Mich. Eichberg,¹⁰ of Cincinnati, reported a case of liver-abscess in the pus of which many amœbæ were found, but no bacteria. In the stools amœbæ were also present in moderate numbers. He also mentions that amœbæ have been found in two other cases of hepatic abscess, occurring, presumably, in Cincinnati. Lutz¹¹ has reported three cases from Brazil, and has added

¹ Massiutin: *Centralblatt f. Bakteriologie*, 1887, Bd. vi.

² Hlava: *Centralblatt f. Bakteriologie*, 1887, Bd. i.

³ Cahen: *Deutsche med. Wochenschrift*, July 2, 1891.

⁴ Nasse: *Deutsche med. Wochenschrift*, July 9, 1891.

⁵ Osler: *Bulletin of the Johns Hopkins Hospital*, 1890, i.

⁶ Stengel: *Medical News*, November 15, 1890.

⁷ Musser: *University Medical Magazine*, December, 1890.

⁸ Rhein: *Medical News*, January 9, 1892.

⁹ Dock: *Texas Medical Journal*, April, 1891.

¹⁰ Eichberg: *Medical News*, August 22, 1891.

¹¹ Lutz: *Zur Kenntniss der Amœbenenteritis*. *Centralblatt f. Bakt.*, 1891, x.

some just criticisms of our inexact classifications of intestinal affections. Wasdin¹ reports a case of dysentery, with autopsy from Charleston, in which many amœbæ were found in the stools and intestinal contents. This case originated in Savannah, and was thought to have resulted from drinking Savannah river-water. I reported² three cases of chronic dysentery, with the usual symptoms, in the stools of which amœbæ were found in large numbers, differing in no essential particular from those described by Osler, Dock, and others. Fitz and Gerry³ report a case of dysentery, with amœbæ in the stools, occurring near Boston. Preston and Ruhräh⁴ report a case of amœbic dysentery from Baltimore; the patient spontaneously recovered. Stockton⁵ reported a case from Buffalo in 1894. Wilson,⁶ of Birmingham, recently reported four typical cases of this disease. A very interesting case of abscess of the liver, which contained amœbæ, complicating amœbic dysentery in a negro boy, has been reported by Slaughter,⁷ of Theological Seminary, Virginia. Lewis⁸ has recently reported a case from Baltimore.

Within the last two or three years numerous articles have been published, both in this country and abroad, on this subject. From England a case has been reported by Curnow,⁹ which originated in India; others who have written on this subject are Tenoglia,¹⁰ Wesener,¹¹ Kovács,¹² Epstein,¹³ Posner,¹⁴ Schuberg,¹⁵ Kruse and Pasquale,¹⁶ Roos,¹⁷ Vivalvi,¹⁸ Celli and Fiocca,¹⁹ and Manner.²⁰

By far, however, the most valuable contribution which has been made to this subject is the monograph of Councilman and Laffeur,²¹ at that time of the Johns Hopkins Hospital.

As a basis for their study they reported fifteen cases (Osler's case included), with autopsies in eight. These careful observers conclude as a result of their studies, together with those of Loesch, Kartulis, Hlava, and others, that the form of dysentery especially characterized by the

¹ Wasdin: *Ibid.*, December 3, 1891.

² Harris: *Ibid.*, December 3, 1892.

³ Fitz and Gerry: *Boston Medical and Surgical Journal*, December 3, 1891.

⁴ Preston and Ruhräh: *New York Medical Journal*, November 10, 1894.

⁵ Stockton: *International Clinics*, 1891, i.

⁶ Wilson: *Johns Hopkins Hospital Bulletin*, September and October, 1895.

⁷ Slaughter: *Virginia Medical Monthly*, October, 1895.

⁸ Lewis: *Maryland Medical Journal*, June 13, 1896.

⁹ Curnow: *Leonard's Illustrated Medical Journal*, January, 1896.

¹⁰ Tenoglia: *Entéro-Colite par amœba coll.* *Archiv. ital. de biol.*, 1890, xiv.

¹¹ Wesener: *Centralblatt f. allg. path.*, 1892, iii.

¹² Kovács: *Beobacht. über Amœbendysenterie.* *Zeitschr. f. Heilk.*, 1892, xiii.

¹³ Epstein: *Prag. med. Wochenschrift*, 1893.

¹⁴ Posner: *Berliner klinische Wochenschrift*, 1893.

¹⁵ Schuberg: *Centralblatt f. Bakt.*, 1893, xiii.

¹⁶ Kruse and Pasquale: *Zeitsch. f. Hyg.*, 1894, xvi.

¹⁷ Roos: *Arch. f. exp. Path.*, 1894, xxxiii.

¹⁸ Vivalvi: *Riforma Med.*, 1894, No. 188.

¹⁹ Celli and Fiocca: *Centralblatt f. Bakt.*, 1890, Bd. ix. u. x.

²⁰ Manner: *Wiener klinische Wochenschrift*, February 20, 1896.

²¹ Councilman and Laffeur: *Johns Hopkins Hospital Reports*, ii., Nos. 7, 8, and 9.

amœbæ in the stools "is a form of dysentery which etiologically, clinically, and anatomically should be regarded as a distinct disease."

My observations on this disease embrace the clinical study of thirty-five¹ cases—the details in three having been already published—and the post-mortem appearances in five.

Below is given a brief *résumé* of the clinical histories of these cases, the complete details being rather too tedious for publication. I desire to emphasize the fact that most of my cases were chronic. Thirty-one of my thirty-five patients with this disease were born in America, and four were of foreign birth. Of the former, eighteen were white and thirteen were negroes. Of the latter, all were Russian Jews. Of the thirty-five patients, four were under ten years of age, five from ten to twenty, five from twenty to thirty, eleven from thirty to forty, six from forty to fifty, and four from fifty to sixty at the time of the onset of the disease. Thirty of the patients contracted the disease in Atlanta Ga.; one in Decatur, Ga.; one in Athens, Ga.; one in Talladega, Ala. and two in Chattanooga, Tenn. Six lived in fairly healthy localities, while twenty-four resided in very unhealthy localities; the conditions under which five lived were not known, but with one exception were probably bad. Four denied drinking well-water at all, while thirty obtained their drinking-water from surface wells; in one case nothing was learned of the source of water-supply. In two instances two of the patients were taken simultaneously while living in the same house, and in one instance three were taken under the same circumstances. Twelve were laborers; many of the women had no occupation, and several worked at the ordinary trades. With but few exceptions the patients were from the lower walks of life. Nothing of importance developed from inquiries as to their family histories. Six had had dysentery before.

Of the thirty-five cases two were developed in March, one in April, seven in May, five in June, five in July, seven in August, four in September, and four in December. In eighteen of the cases the onset was slow, and in sixteen the disease began as a severe dysentery; the nature of the onset in one case was not determined. Twenty-three lost flesh decidedly.

After the disease becomes chronic the temperature is usually slightly elevated, especially at night, but rarely goes above 101° F. Both pulse and respiration are normal, or but little accelerated. The tongue was more or less coated in twenty-five cases; it was also often slightly reddened at the edges. Edema was noted under the eyes in two cases, and under both eyes and around the ankles in four. In eight instances the abdomen was distended; in one it was retracted; it was tender in eighteen instances.

¹ Five of these cases were seen after the paper was read.

Sugar was not found in the urine of any of the cases, and albumin only once. Peptones, albumose, and globulin were carefully searched for in several bad cases, but none found. When the stools are excessively watery and copious, chlorides largely disappear from the urine; in one case there was total suppression of chlorides for a time. The number of stools vary from two to forty, or even more, in twenty-four hours. They vary in consistency with the varying severity of the disease. In nine cases they were very watery; in three, semi-fluid; in twenty-one, semi-solid; in one, nearly solid; and in one case undetermined. In color they vary somewhat, but in over half of the cases they were pink, reddish, or reddish-brown; rarely are they of the normal yellow color. With scarcely an exception, they were exceedingly offensive. The reaction in the first few cases was not determined, but subsequently all examined were found alkaline, except in two instances. In six analyses of the stools in two severe cases large quantities of serum albumin were found, and small amounts of peptones (Hofmeister's method) were found present in each specimen examined. Neither globulin nor albumose was found, but that small quantities were present can scarcely be doubted. Chlorides were largely present. On microscopic examination, all were found to contain, in addition to the usual undigested particles of food, pus-cells, more or less red cells, large epithelioid cells, multitudes of bacteria, and amœbæ. In six instances *Cercomonas* were found, and in one *Trichomonas*; in one case (a child) the eggs of *Oxyuris vermiculosis* were found.

All complained of more or less griping and frequent desire to go to stool. Abdomen was more or less constantly painful in fourteen instances, and eight complained of backache; the backache was continuous in some of the cases, but in others intermittent—in two cases being aggravated by the recumbent posture. Four of the patients complained of nausea and vomiting, three of night-sweats, and five of fever and thirst. Obstinate hiccough was observed twice preceding death.

As complications, liver-abscess occurred twice, peritonitis twice, piles once, and appendicitis once.

Ten were treated with the ordinary astringents; two of these recovered, five died, and the result in three is unknown; one of the recoveries occurred while the patient was taking bismuth subnitrate and opium, and in the other case the result was spontaneous. Twenty-five were treated by rectal injections of solutions of hydrogen dioxide; eight recovered, four improved, two were not benefited, five died, and the result in six unknown. One recovered under injections of solutions of potassium permanganate, and another recovered while under the care of another physician. Of my thirty-five cases twelve recovered, four improved, nine died, and the result in ten is unknown.

Like the symptoms and the effects of treatment, the duration is ex-

tremely variable; one case died in eleven days; when last heard from, some had existed half as many years.

ETIOLOGY. Amœbic dysentery is a disease pre-eminently of the poor, and is almost always associated with filth, bad hygienic surroundings, and lack of proper food; hence it is that it is very rare in the country and smaller towns, but here the catarrhal form is quite frequent. Where the matter has been inquired into, it has been also found that, in a large proportion of cases, the patients had been more or less in the habit of drinking surface drainage water from wells; this was found to be true in thirty out of my thirty-five cases. As a predisposing cause, race seems to be an important factor, as out of the seventy-eight cases reported in this country (the ones I now report being included), only eighteen have occurred in the colored race. A considerable number have also occurred in foreigners. The infrequency with which it occurs in children and young adults is very remarkable—the proportion being about ten grown persons to one under twenty-one years of age. It seems to occur in males about three times as frequently as in females. Although it occasionally begins in the winter, the onset is almost invariably in the summer months—especially in May, June, July, and August. In this it differs markedly from the catarrhal form, which, in the South, is certainly more frequent in the early spring months. Attempts to connect any special form of bacterial life with this disease have heretofore proved futile, but a parasite belonging to the great group of protozoa has been found in the intestinal lesions with great uniformity. It cannot be denied, however, that positive proof of the etiologic relation of these organisms is still wanting; but when we consider that amœbæ, the descriptions of which, from all sources, differ very slightly, have been found constantly present in the stools of a common, chronic, and very fatal form of dysentery, in various parts of Europe, Asia, Africa, and in both North and South America, and that they occur in the stools of other diseases certainly very rarely—which might be easily accounted for by supposing some complicating amœbic pathological process—it is strong presumptive evidence that they play an important rôle in the production of the pathologic changes which occur in this disease; when we further consider that competent observers have always succeeded in demonstrating these organisms in and around the ulcers which occur in the colon, and that one observer, by the rectal injection of cultures of the amœbæ, has produced inflammation and erosion of the mucous membrane of the large intestine of lower animals, the evidence becomes even stronger that they are the active causative agents in this affection. Further, large numbers of amœbæ—sometimes occurring in pure cultures—are found in abscesses of the liver and lungs, complicating amœbic dysentery. Flexner,¹ in

¹ Flexner; Johns Hopkins Bulletin, September, 1892.

a very interesting article, describes amœbæ occurring in the pus from an abscess of the lower jaw, which he regards as "allied species if not identical" with the amœbæ dysenterie.

In collecting the feces for examination for the amœbæ, some precautions are necessary to prevent the death of these organisms before the examination is made, as, when dead, they resemble very much the large epithelioid cells which often occur so abundantly in dysenteric stools; the stools should be received directly in a perfectly clean vessel, which in cold weather may be warmed, and should contain no water or other fluids, urine being especially damaging. The amœbæ are from twelve to thirty-six micromillimetres in diameter. Generally the body of an amœba can be distinguished as being made up of an outer, clear homogeneous substance or ectosarc, and an inner, highly refractive mass or endosarc; within the latter are found foreign bodies, such as bacteria, granular detritus, bodies which seem to be red blood-corpuscles, and one or more large vacuoles, and great numbers of smaller ones, giving the appearance of granulation; they are frequently found, however, with few or no vacuoles of any size. The impression has gradually grown upon me that amœbæ in each case bear a general resemblance to each other in respect to the number and size of their vacuoles, or at least it is true for comparatively lengthy periods, if not throughout the entire course of the disease. Within the vacuoles, bodies in active Brownian movement may be sometimes seen. In consistency the ectosarc is semi-solid, allowing the amœbæ to push readily through the granular débris found in the feces, but the endosarc must be quite liquid, for on one occasion, within the body of one of these organisms, which was almost entirely free of vacuoles, an actively moving bacillus was seen. When dead, before disintegration begins and when not active, the organisms are generally round or nearly so, but occasional exceptions are seen. When in motion almost every conceivable form is assumed, barring that the irregularities of the amœbæ body and the processes sent out are invariably rounded. Progression of the amœbæ may be accomplished by a steady crawling movement, or, what is more usual, pseudopodia are sent out, followed by the contents of the body flowing into them, which causes a rapid increase in the size of the pseudopodia and continues until the entire body changes place. While living, the amœbæ are not affected by currents under the cover-glass, but when dead they drift like other inanimate particles of matter. The cell contents frequently change place without perceptible movement of the ectosarc. While moving, a collection of fecal detritus is often attached to the posterior portions of the amœbæ, and frequently I have been unable to make out the exact point of separation; indeed, it has seemed to me, at times, that there was direct continuation of one into the other. If this is true it may explain what has always puzzled me—i. e., how do the amœbæ take in their

food and the various cellular elements which are almost always found in their bodies? In this connection, the observations of Cienkowski¹ Duncan,² Leidy,³ and Cunningham⁴ on this subject are of great interest. As far as my observations go, pseudopodia are never sent out at the point at which these masses are attached to the amœbæ. The bodies of the amœbæ usually have a faint green or bluish-green color. A nucleus may sometimes be distinguished in them, but by no means always; it is usually surrounded by a white rim; they sometimes change their form slightly. No contractile vesicle was ever seen.

The length of time that they live after being passed varies considerably in each case; amœbæ from Case I.⁵ often remained alive and active for twenty-four hours in a room where the temperature fell almost to the freezing-point during the night; this, however, I regard as being very exceptional. As a general rule, they die in from two to six hours after expulsion from the intestine. Writers on this subject have claimed that temperature exerted a marked influence on the length of time which they would live, but, while believing that a temperature about that of the body is most favorable to them, I have so far seen nothing to convince me of the truth of the above conclusion. I have often noticed that, from the same case, amœbæ died about as soon at the temperature of the room as when kept at 37° C. in an incubator. My experiments to determine the toxic effects of various agents on amœbæ have been confined largely to Case I., in which, as above indicated, the amœbæ seemed unusually tenacious of life. The organisms in this case were not killed in any reasonable length of time by lowering the temperature of the fluid in which they were contained to 0° C.; neither were they seemingly at all affected by saturated solutions of quinine sulphate or boric acid—both of which have been recommended for the purpose. A 1:300 aqueous solution of quinine bisulphate invariably killed the amœbæ within ten minutes. They are killed by weak solutions of hydrogen dioxide, potassium permanganate, and toluidine blue; they are also killed by acids, even when very dilute, and for this reason, largely, the urine acts in a similar manner, but its toxic effect is not entirely due to its acidity, as I have found that after being neutralized the amœbæ do not live very long in it. Agents, rectal injections of which were likely to prove harmful to the individual, were not experimented with.

As shown by me,⁶ the amœbæ sometimes reproduce after being ex-

¹ Cienkowski: *Archiv f. mikrosk. Anatomie*, 1865, Bd. I. S. 303.

² Duncan: *Popular Science Review*, 1877, p. 217.

³ Leidy: *Fresh-water Rhizopods of North America*, p. 27.

⁴ Cunningham: *Quarterly Journal of Microscopic Science*, 1881.

⁵ For convenience, the cases are referred to in this paper in the order in which they were seen.

⁶ Harris: *Medical News*, November 24, 1894.

pelled from the intestine; multiplication takes place by direct division. Attempts to cultivate them in straw infusions, as recommended by Kartulis,¹ have always been unsuccessful.

For a long time I was unable to find a stain which would color the amœbæ in the fresh state, as they showed not the slightest tendency to take any of the ordinary dyes. Some progress was made by adding to the fresh cover-slip preparations of fecal matter a drop of an aqueous solution of acid fuchsin, which has the effect of coloring deeply all objects ordinarily found in the stools except such crystalline bodies as might be present and the amœbæ. After having discovered the great affinity that toluidine blue displayed for the fixed amœbæ, at the first opportunity I added a drop of watery solution of this substance to a small particle of the feces, and examined it immediately under the microscope; here, as in the tissues, the endosarc of the amœbæ was always intensely stained at once; the ectosarc only becoming so after the lapse of several minutes. In fresh preparations the ecto- and endosarc are beautifully differentiated. The amœbæ seemed to be instantly killed, and often their natural forms were beautifully preserved. The cover-slips, after being washed in water and mounted in Farrant's medium, may be preserved for many months, but after a time the preparations completely fade. It is evident that in addition to staining the dye also acts as a fixative. Weak solutions of the stain should be used, or the cover-slip should be washed in water before mounting. In staining the feces by this method, frequently small, vacuolated bodies were found which take the stain as do the amœbæ; these bodies are about the size of leucocytes, but differ from them in many particulars.

Attempts were made to stain the amœbæ in cover-slip preparations of the feces by first placing both the dried and moist cover-slips in various hardening and fixing solutions. Alcohol, both weak and strong, Müller's solution, strong solutions of potassium permanganate, 2 per cent. osmic acid solutions, strong and weak solutions of chromic acid, Hermann's solution, Flemming's strong solution, and Heidenhain's mercury bichloride salt solution, with a little acetic acid added, were all tried, with but very indifferent results—the last three, however, giving the best. By none of the methods were they sufficiently well preserved to present more than a very faint resemblance to these organisms when alive; none of the above agents killed rapidly enough to prevent enormous shrinkage and the bodies of the amœbæ from losing their more or less characteristic irregular form and becoming rounded. Scarcely better results were obtained from sections of fecal masses, which were treated with the above hardening agents, embedded, cut, and stained.

¹ Kartulis: "Einiges über die Pathogenese der Dysenterieamœben." *Centralblatt f. Bakteriologie*, 1891, Bd. ix.

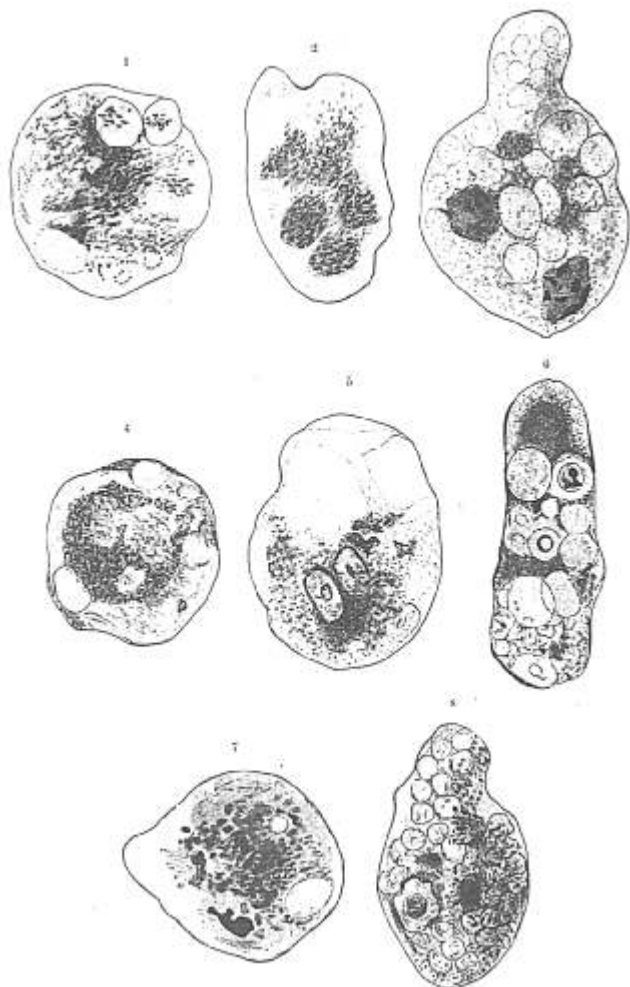
Strangely enough, and this fact is mentioned by Councilman, the amœbæ are much better preserved by hardening agents in the tissues than in the feces; but even here, in the most favorable cases, they shrink considerably, and generally lose largely their characteristic vacuolation; the only explanation of this fact which has occurred to me as being at all likely is that the solutions do not reach the amœbæ at first in so concentrated a form as when merely the feces are used; but this, it must be admitted, is a mere assumption without any real proofs, and which even seems unlikely when it is remembered that the results are practically the same whether great or small masses of feces are used.

The amœbæ were well preserved in the tissues when acidified Heidenhain's mercury bichloride salt solution, Hermann's solution, Flemming's solution, Müller's solution—made very strong and placed in the incubator for three days, as recommended by Councilman—and alcohol were used as hardening agents—the first three, as in the case of the feces, giving the best results. A large number of staining reagents were used on the tissues hardened in each of the above solutions, with varying results. Councilman states that the amœbæ are probably most easily distinguished after hardening in alcohol and staining with Loeffler's methylene blue; I would add that results quite as good, if not better, are obtained with this stain by fixing in corrosive sublimate, instead of hardening in alcohol. Now, while the amœbæ are brought out very prominently by the above stain, it is by no means to be recommended for studying the delicate internal structure of these organisms, as the entire endosarc seems to take up nearly the same amount of the stain, and their bodies become so dark that the vacuoles are no longer apparent, and the nuclei are not distinguishable with certainty. The iron hæmatoxylin of Buetschli gives much the same general effect, the only difference being that they stain darker. After fixing in any of the above reagents the amœbæ are especially well stained by blue solutions of hæmatoxylin, but the same objection applies in this case as was mentioned in connection with methylene blue, namely, that the amœbæ were so intensely colored that the internal structures could not be observed; fairly good results were obtained by first staining with hæmatoxylin and after with eosin, benzopurpurin, or picric acid, the last three, however, always washing out the first rapidly. After hardening in Heidenhain's solution, they stain brilliantly in the carmines, but not quite so dark as the tissues; very beautiful and delicate stains were obtained with weak alum carmine containing a trace of osmic acid. The amœbæ stain fairly well by Bizzozero's modifications of Gram's gentian violet aniline-water method; staining first with gentian violet, and following with eosin, gives much the same effect, but I fancy somewhat better than hæmatoxylin and eosin; the nuclei are beautifully stained in this way. Nigrosin stains the bodies of the amœbæ well, but the nuclei are

not brought out. The Ehrlich-Biondi-Heidenhain stain produces delicate but very faint results. I have never seen the nucleus stained by the methylene green of this combination, but strangely, the ectosarc of the amœbæ stain faintly with this color; this stain works best with corrosive sublimate objects. Victoria blue stains the nuclei faint blue; no other part of the organism is at all colored, however. The bodies of the amœbæ stain yellow by Van Giesens' method; the nuclei are faintly stained. Very fine results were obtained by staining with carbol-fuchsin, the bodies of the amœbæ stain a beautiful purplish red, the borders and centres of the nuclei being a dark purple; the stain is perhaps somewhat more decided after hardening in osmic acid solutions. Safranin stains the endosarc a reddish color, some parts looking, however, quite dark; the irregular nuclei are stained dark in the centre and at their margins, and the ectosarc faintly red; perhaps no method shows the division of the amœbæ into endo- and ectosarc so well as this one. Equally good, if not better, results in some particulars are obtained by first staining lightly with hæmatoxylin and after with safranin, according to the method of Rabl. Flemming's orange method gives very fine results—the nuclei being very distinct and the protoplasm darker than when safranin is used alone. It is noteworthy, as is the case with the tissues, that all safranin stains are fainter and less precise when the amœbæ have been hardened with corrosive sublimate than when hardened in osmic solutions. The bodies of the amœbæ are slightly and the nuclei very decidedly stained by Weigert's fibrin stain.

Although very fine stains may be obtained by some of the above methods, decidedly the best results, so far as the internal structure of the organism is concerned, have been obtained by hardening in corrosive sublimate and staining in Heidenhain's iron alum hæmatoxylin; the method gives a dark, very transparent, and highly differentiated coloration, but permits the vacuoles to be seen as in no other stain; the nuclei are irregularly stained, being darkest on the periphery and at their centres. Furthermore, the amœbæ, when stained by this method, can be detected in the tissues almost as readily as if stained by methylene blue, and are much more easily distinguished from objects resembling them. When the above method is used the amœbæ very frequently closely resemble those in a living state, the only difference being that there is always more or less shrinkage. (Fig. 1.)

Having observed the fact, as already mentioned, that the protoplasm of the amœbæ exhibited marked affinity for the blue solutions of hæmatoxylin and methylene-blue, it occurred to me that perhaps the endosarc of the amœbæ was composed of a mucus-like substance; I therefore stained some specimens of intestine containing these organisms, which had been fixed in corrosive sublimate, with a weak watery solution of toluidin blue, and found the amœbæ were much more deeply



Amoeba and a cell from the margin of a liver abscess. Toluidin-blue and eosin; Zeiss $\frac{1}{12}$ oil immersion, Oc.C. Nos. 1, 5, and 8 were fixed in Hermann's solution; Nos. 2, 3, 4, 6, and 7 were fixed in corrosive sublimate. No. 1 was stained by Flemming's safranin, gentian-violet, and orange stain; No. 5 by Robb's haematoxylin-safranin method; No. 8, which is a degenerate liver cell, and is put here for the purpose of comparison, was stained with carbol-fuchsin. Nos. 2 and 4 were stained by Loeffler's methylene blue. Nos. 3, 6, and 7 were stained by Heidenhain's iron-haematoxylin method.

stained than the tissues. After experimenting further it was observed that a beautiful contrast stain could be produced by staining first in eosin or benzopurpurin, and after, for twenty or thirty minutes, in a weak solution of toluidin blue; the excess of the latter stain is washed out with alcohol, which usually takes three or four minutes, and the section is then cleared in cedar oil or xylol, it having been found that other clearing agents more or less injured the stain. If the sections are washed in alcohol for only a short time the amœbæ are stained a very solid dark blue, in which their nuclei can be seen stained of even a darker color, but if the washing is prolonged their bodies are not so dark and have a reddish tinge, the vacuoles becoming quite distinct, and the outer portions of the ectosarc retaining the pigment very slightly; the tissues are a purplish red, while the nuclei stain very nearly the same color as the amœbæ. If the eosin is used after the toluidin blue this stain is washed out of the amœbæ. By this method it is possible to examine with a low power a large section for these organisms in a few moments. It is certainly by far the most beautiful stain yet discovered for the amœbæ; indeed, it would be hardly possible to devise a better. It seems quite likely that the endosarc is made up of a substance greatly resembling mucin, and the inference is not without justification that the endosarc of other rhizopods and other members of the protozoa may be also composed of a like material, and may give the same reactions with toluidin blue. It kills *Cercomonas* quickly, but scarcely stains them at all. Although somewhat out of place, I would call attention to the fact that the combination of eosin and toluidin blue is a most excellent method for general histologic work, and compares favorably with the results obtained by staining with eosin and hæmatoxylin or gentian violet. Unfortunately, the stain gives differential effects only with corrosive sublimate or alcoholic objects. Other mucin stains, as thionin, muchæmatein, and mucicarmine, were tried, with excellent results, but none gave such fine effects as the toluidin blue; the results with thionin were especially good, but the stain cannot be used with eosin and the like, as it will not replace these acid dyes in the amœbæ. In this connection it may be noted that hyaline cartilage, mastzellen, and the jelly of Wharton give the same reaction with basic dyes as mucin does.

From the above, it will be seen, as should have been expected, that the bodies of the amœbæ have much more affinity for plasmatic than for nuclear stains, and that the latter are always washed out by the former. Within the bodies of the amœbæ may be generally seen some granular detritus, the result, no doubt, of cellular disintegration; but I have found it extremely difficult, after staining, to recognize with any certainty included cells. Neither have I in a single instance been able to make out the radiate-like structures described by Councilman as sometimes occurring in the protoplasm of these organisms; the fluid nature

of the endosarc would seem to make very improbable the existence of these structures during life, and when it is remembered that they were found only in tissues hardened by Flemming's solution, which contains a large proportion of chromic acid, the possibility is strongly suggested that they may be artefacts. I have never seen fat in the interior of the amœbæ.

The question as to how the amœbæ gain access to the system is one of great interest, and a perfectly satisfactory answer has, as yet, not been given. In all of the cases reported by Councilman and Lafleur the patients were drinking well-water at the time of the onset of the disease, and with but three exceptions—and even here it is a matter of doubt in two of these—the same is true of all my cases. Of great interest in this connection is the case reported by Fitz and Gerry, as these observers demonstrated the presence of amœbæ, in most respects resembling those found in the feces, in a cistern from which the patient constantly used water. A careful examination of the water used by patients in Cases XII. and XXIV. failed to reveal the presence of amœbæ; neither were they found in the mud from the bottom of the wells or scrapings from the well-bucket.

PATHOLOGICAL ANATOMY. On opening the abdominal cavity in Case IV. several localized sacs of pus were found; and from an ulcer which penetrated through the entire thickness of the gut there was a general peritonitis; this was also found in Case XIV. There was a considerable amount of pus found in the peritoneal cavity, in both cases of a whitish-yellow color. In Case IV. there were adhesions of the large intestine to all contiguous objects; the gut was much distorted, being drawn in first one direction and then another, as was also the small intestine, which was fastened to it wherever they came in contact. Most of the adhesions were old and very firm. The large intestine was at some points enormously thickened; at others so thin that it was impossible to avoid many tears during its removal. In all cases the intestinal contents consisted of a mass of foul-smelling semi-solid fecal matter, of a dark-brown color, containing particles of undigested food, blood, and much mucus. Amœbæ in the feces were sought for only in Cases XIV. and XXII., and were found in both. The characteristic lesions in this disease are the ulcers of the large intestine. These ulcers may extend almost continuously from the rectum to the ileo-cæcal valve, or may be confined to one or more limited areas. Rarely, as in Case XIV., the ulceration may extend into the small intestine. A novel feature, which I have not seen mentioned in reports of others, is that the appendix was also involved in this case. This appendage was found surrounded by pus, which contained amœbæ, was much enlarged, and was bound, for its full length, to the small intestine by firm adhesions. At one point the walls had been completely destroyed,

thus establishing a communication between its cavity and that of the surrounding abscess. On section, the appendix was found filled with thick whitish pus, in which many amœbæ were found. The ulcers are found in greater number on the lower and anterior part of the gut. It was especially noted, in all cases, at the points where the mesocolon was attached, and where the guts were fastened to the sides of the abdominal walls, that ulceration was practically absent. The ulcers are sometimes round or irregularly shaped, but are generally oblong, and lie transverse to the long axis of the colon; a form of the latter very frequently seen begins an inch or an inch and a half from the attached part of the gut, with a rounded extremity, and tapering somewhat, becoming lost near the point just named in several irregular continuations which follow the depressions between the numerous rugæ in this situation. They vary very much in size—some being no larger than the head of a pin, while others are sometimes as much as two inches in diameter. In the larger ulcers the muscular coats are frequently dissected up for some distance. These masses of muscular tissue sooner or later become detached, and are found in the stools as sloughs. In none of my cases was that honeycombing of the tissues observed that Councilman and others have described, but it was usually the case that the edges of the ulcers were somewhat undermined.

When sections of the intestine are examined with the microscope, the walls are usually found normal at a short distance from the edge of the ulcer. Approaching more closely, either one or the other of two changes may be first observed: either the submucosa shows marked changes, with the mucous membrane above practically normal, or the mucosa may be eroded and no abnormality beneath.

In the former, which is by far the more frequent, and which may be considered the typical intestinal lesion of this disease, changes in the submucosa may be traced in advance of the surface ulceration for quite a distance, thus undermining the comparatively healthy mucosa above. The appearance of these ulcers when fresh is entirely characteristic. A short distance from the point where the ulceration begins the upper portion of the glands of the mucosa are slightly but irregularly eroded. From this point to the edge of the ulcer the cells of the interglandular reticulum are usually slightly increased in number. The most careful search with high powers failed, however, to show any evidence of mitosis. At a short distance from the edge of the ulceration amœbæ are not found in the mucosa, but rarely one or two of the parasites may be seen either within or between the glands just at the margin. More or less marked fatty degeneration of the cells of the mucosa occur, which is always most intense at the edge of the ulcer. The glands contain great quantities of mucus, which become especially marked at the edge of the ulcer. Often from some part

of the margin of the ulcerated mucosa a band—usually at first small—of irregular and ill-formed mucous tissue passes off, which generally becomes larger, and may extend for considerable distances over the ulcerated submucosa, or may be reflected back over the healthy mucous surface. After passing back over the healthy mucosa these bands are often reflected back over themselves—which may be repeated several times. The large bands sometimes divide into two small ones. When growing over the ulcer they seem sometimes to become attached to its surface, but this is very rare in my cases. I have never seen epithelial cells lining the ulcers, as described by Councilman and others. Amœbæ—so rare in the healthy mucosa—are quite frequently present in these outgrowths just described, but appear to exert no influence on the growth or breaking down of these bodies. The bloodvessels of the mucosa are sometimes found greatly distended with blood; but, in my experience, this is always accomplished by a high degree of bacterial infection. At the centre of the ulcers the muscularis mucosæ is always broken down, but it suffers much less than the tissue beneath, and may be often seen to extend in a comparatively healthy condition beyond the mucosa, thus covering the broken-down tissue beneath. The above, no doubt, partially explains why the breaking down of the mucosa does not keep pace with that of the submucosa. That part of the muscularis mucosæ which hangs over the ulcer is swollen, and toward the free end the fibres are granular, and their nuclei are for the most part gone, or entirely absent. That part at the sides of the ulcer, and extending back for some distance, is swollen, and the nuclei are increased in number. Where the ulceration is recent the altered submucosa forms the base of the ulcer. The breaking down here is always irregular, giving the ulcer a ragged appearance. Often almost detached shreds of this necrotic tissue lie on the free surfaces of the ulcers. Amœbæ may sometimes be seen lying on or between these shreds, but they are rarely so numerous as deeper down and along the outer edges of the diseased tissue. The surface of the ulcer is more or less covered with a granular detritus mixed with round cells, and a few epithelial and pus cells. These are not regularly distributed, but are often collected in small masses. Bacteria were also present, but never to the extent that would be supposed. The most common organism is one that morphologically resembles and stains like the colon bacillus. The most marked and characteristic changes are always present in the submucosa. The first change is a great swelling of the tissues. Immediately following there is an infiltration with small round cells, and sometimes a few polynuclear leucocytes are also seen, but these are rare. Frequently present also are large, vacuolated, mononuclear cells, which, on account of their size and general appearance, closely resemble amœbæ. They are scattered through the tissues everywhere, but are most frequent where the disease-process is most actively advancing, and are at these points

often very numerous. They seem to be connective-tissue cells which have absorbed liquids. This assumption is supported by the fact that the connective-tissue cells swell along with the tissues, and may be even seen in all stages of the transformation. They stain a light red with a blue nucleus with the toluidin blue eosin stain. At the margin of the ulcers the protoplasm of these cells often undergoes a sort of parenchymatous degeneration, and at the same time the nucleus swells and becomes indistinct. These cells all stain poorly. Mastzellen are diminished in number in the immediate vicinity of the ulcers. Immediately following the swelling and infiltration of the submucosa the more delicate connective tissues soften and break down, and, usually, in the order named—the veins, arteries, and large bands of fibrous tissue. As soon as changes begin in the submucosa the connective tissues become greatly swollen, quickly lose the power of retaining stains, as when normal, soften, and break down. The large bands, especially, show a tendency to undergo a sort of hyaline transformation at or very near the free surface of the ulcer. I have never found this hyaline change very extensive, nor have I observed it forming a reticulum. Before undergoing the change or breaking down, the large bands of fibrous tissue, like the smaller, become pale and take stains poorly. The elastic tissue does not suffer equally with the collagenous fibres, but remains intact and retains its staining peculiarities long after the surrounding tissues have broken down and disappeared. Perfect bands of this tissue are thus often found lying in masses of granular debris at the very edge of the ulcerated surface. Scattered through the tissues everywhere amœbæ are found, but, as a rule, are most numerous near the points where the most active changes are occurring. Very rarely a single amœba may be found somewhat in advance of the pathological process, but the great mass of these organisms follow, rather than precede, the characteristic changes. They lie almost always in the lymph spaces and in the lymph sinuses, which are numerous in the submucosa. They do, however, occur in the tissues, where a clear zone may almost always be seen around them, which probably results from contraction caused by the fixing agent. No direct local action of the amœbæ can, as a rule, be observed. Amœbæ are also frequently found in the perivascular lymph channels. When amœbæ are present proliferation of the endothelial cells which line the lymph sinuses is often seen. The lymphatics may be considerably, and are often enormously, dilated. Small amounts of fibrin are sometimes found in these sinuses. Masses of fibrin are often found in the tissues just below the ulceration. The walls of the veins are early infiltrated with round cells, quickly followed by softening and complete disorganization. This, no doubt, explains largely the constancy of hemorrhage in this disease. As a rule, the veins contain no more blood than normal. Thrombosis of the veins is not infrequent; but, very strangely,

it seems independent of the presence of amœbæ within the vessels, where they are quite frequently observed. They may occasionally be seen in the act of penetrating the walls of the veins—part of their bodies being within and part without the lumen of these vessels. In like manner the walls of the arteries are infiltrated, and there is evidence of endarteritis, more or less pronounced, as the ulcerative process is slow or rapid. In chronic cases the lumen of the arteries may be entirely occluded by this process. The walls of the vessels sometimes undergo the same hyaline change which occurs in the connective tissue, generally beginning on the side nearest the ulceration. Before the ulceration reaches the muscular layer the nuclei of the fibres swell up, become more oval in shape, and greatly increase in number. After the ulcerative process passes through the submucosa the inner muscular layer, for a time, checks the further progress of the disease. The amœbæ, however, soon force their way into the intermuscular septa, and here cause the same changes which are produced in the connective tissues above. Simultaneously the connective tissue envelope of the muscular layer, which lies next the submucosa, breaks down, and the amœbæ penetrate between the individual fibres. In none of the other tissues are the local effects of the amœbæ more pronounced, and in none can the changes produced be so accurately observed. As with the submucosa, the swelling is pronounced, but with the difference here that the amœbæ precede or keep pace with this condition. The mechanical effect of these organisms on the fibres is always at once obvious. The cement substance softens and gives way, and the amœbæ pass onward between the fibres, pushing them to either side. The fibres swell somewhat, and soon soften, become granular and indistinct, lose their nuclei, and finally entirely break down. The bloodvessels of the muscular layer suffer the same changes which occur in those of the submucosa. As soon as the amœbæ force their way through the circular muscular layer, they pass outward in all directions, and immediately there follow the same swelling, infiltration, and necrosis of the tissues between the two muscular coats, which, under similar circumstances, occur in the submucosa. In the same manner the bloodvessels are destroyed, and, in addition to the already existing disease-producing causes, there follow those changes which result from cutting off the blood-supply. In this way quite extensive sloughs may occur. In the longitudinal muscular coat there is found an exact repetition of the changes which are produced in the circular layer. While the amœbæ are still in the muscular coats, and before any of them pass entirely through, the bloodvessels of the subperitoneal coat become engorged with blood, there are small round cell infiltration, swelling of the tissues, and, in fact, all the phenomena which precede the amœbæ in the submucosa, except that here there is always considerable connective tissue hyperplasia. After the amœbæ reach this coat there may be ob-

served the same necrosis of the tissues and breaking down which occurs in the submucosa. This process may extend outward, and a portion of the peritoneum, becoming necrotic, sloughs out, causing perforation into the peritoneal cavity. More usually, however, the peritoneum thickens more rapidly than the necrotic process advances, which often continues until an enormous thickening of this coat results. Fibrin formation is especially frequent on the peritoneum and in the subserous coat. It is a notable fact that the hyperplastic tissue which is produced in this disease is much more resistant to the disease-producing cause than are the original tissues. The question as to how the amœbæ reach the submucosa is one of great interest. Councilman thinks that they penetrate the mucosa and muscularis mucosæ, and then produce the highly characteristic lesions which always accompany their presence. This certainly seems the only probable hypothesis, if we reject the possibility that the disease may begin as a catarrhal inflammation, and that later the ulcers become secondarily infected with the amœbæ—a supposition that the microscopical anatomy of the ulcers seems at once to refute. On the other hand, it should not be forgotten that the amœbæ penetrate mucous and muscular tissue only with great difficulty, and that they are rarely found in these tissues—especially in the former. In chronic cases, adhesions of the gut to neighboring objects is quite frequent, and, as a result, great distortion sooner or later follows. When these adhesions connect with the small intestine, deformities, almost as great, occur also in this. In some cases the ulcers do not follow throughout a typical course. In Case VI., particularly, were found many ulcers which extended only a short distance below the mucous membrane, and in which there was an absence of most of the phenomena above enumerated. The fibrous tissue of the submucosa in these ulcers was considerably thickened, and bore a striking resemblance to the new-formed fibrous tissue of the peritoneum already referred to. Many amœbæ were found in this tissue, but seemed to exert little, if any unfavorable action upon it. Amœbæ were found in the walls of the ulcers of the ileum and appendix in Case XIV. (Figs. 2 and 3.)

The other form of ulceration, spoken of above, was found only in Case XIV., but seemed quite as frequent as the more typical form in this instance. These ulcers increased in size by gradual softening and breaking down at the surface—never by necrosis and sloughing of the underlying tissues. They sometimes do not extend deeper than half through the mucosa, but generally reach into the submucosa, and rarely extend to the circular muscular layer, but never deeper. They are characterized by the fact that they are more properly a lesion of the mucosa, any deeper ulceration being apparently secondary, and that there is never that swelling and infiltration of the submucosa in advance of the breaking down which characterizes the ulcers already spoken of. Further-

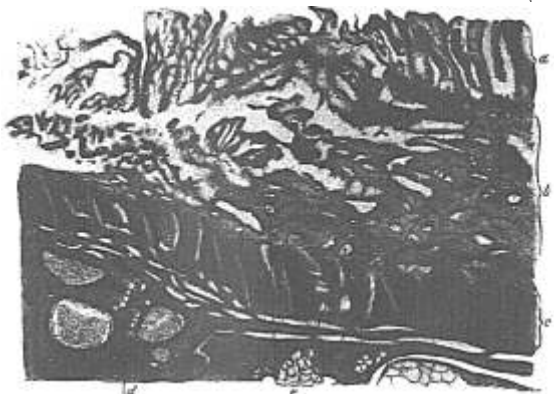
FIG. 3.



Section of intestine just below ulceration. Toluidin-blue and eosin. Beck $\frac{1}{4}$, Oc. 3. In upper portion of the field a large vein is seen; the wall of the vessel which is nearest the ulceration is being infiltrated with small cells and is breaking down; both red and white cells and amœbæ are seen within the lumen of the vessel. In the lower portion of the field many amœbæ are seen, some in the tissues, and others in the lymph spaces and lymph channel.

more, *they never contain amœbæ*. That abrupt breaking down of the mucosa at the margin of the ulcers which is so common in the other variety is here extremely rare, and never is there that undermining of the mucosa or that luxuriant proliferation of mucous tissue which is almost invariable in the other case. On the other hand, the mucous surface is more or less eroded for some distance from the deepest part of the ulcers, and the glandular epithelium beneath is usually entirely gone or lying in loose masses in the cavities they formerly lined. The blood-vessels are, moreover, more completely distended with blood than is usual in the other variety of ulceration. When the breaking down

FIG. 2.



Edge of intestinal ulcer. Toluidin-blue and eosin. Beck 1 inch, Oc. 3. *a*, mucous coat, which projects over ulcer at *f*; *b*, submucosa; *c*, circular layer of muscle fibres; *d*, tissues of mesocolon; *e*, amœbæ in dilated lymph spaces.

extends into the submucosa there is comparatively little swelling of the tissues, but the small round-cell infiltration is more pronounced than is the case with the ulcers first described. The large, swollen connective-tissue cells, which are so numerous in the other ulcers, are never here observed. The chronic nature of the process in these cases is shown by the fact that there is a decided increase of the fibrous tissue in the neighborhood of the ulcers. The walls of the bloodvessels suffer but little change, and break down only when they are actually reached by the ulceration. The vessels are usually distended with blood. Hyaline changes were never found, either in the tissues or in the walls of the bloodvessels. The lymph vessels are not dilated, nor is there any

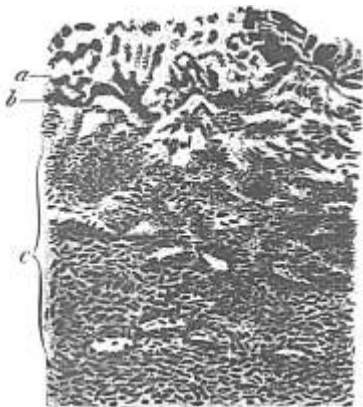
marked change in their walls in advance of the general breaking down of the tissues. After the ulceration reaches the circular muscular coat the number of nuclei in the fibres is sometimes increased, but is never so decided as in the former variety. Under like conditions, the inter-muscular septa may become thickened.

The lymphatic glands of the large intestine in Case XXII. were found somewhat swollen, but were not hard. On section, they presented the usual appearance. Pieces were fixed in corrosive sublimate and Hermann's solutions. Sections were stained by the same methods which were used in staining sections of the intestine. On microscopic examination the lymph sinuses were found considerably dilated, and contained numerous large, swollen cells which almost always contained one, and more frequently numerous vacuoles. These cells usually have only one nucleus, but there are frequent exceptions. Mitosis can sometimes be observed. These cells have occasionally no nuclei, but in these cases the protoplasm takes the stain poorly, and the entire cell is evidently undergoing degeneration. The protoplasm of these cells is acidophilous, and hence shows a red coloration with a dark nucleus when stained by the eosin toluidin blue method. They resemble in every particular the swollen connective-tissue cells which are so numerous in the vicinity of the ulcers, and, like them, greatly resemble amœbæ, especially when stained by some methods. They contain no fat. The lymphocytes of the glands are probably somewhat increased in number. No change of the reticulum or of the bloodvessels is observed. The glands in Case XXXV. were also swollen. They showed a decided increase of lymphocytes and a few of the above-mentioned cells.

In Case XIV. there was an hepatic abscess. The liver was pale in color and was considerably enlarged. It was attached firmly to the diaphragm wherever in contact with it. At one point the ulceration had extended through the capsule of the liver, and almost through the diaphragm. On section, the right lobe was found to be almost completely destroyed, the capsule constituting at many points the only wall of the abscess. One abscess of considerable size and many small ones were found scattered through the left lobe. The inner walls of all of these abscesses are very irregular, and in the larger ones present an extremely ragged appearance. It is a curious fact that these abscesses, as in the present instance, show a much greater tendency to rupture into the lung than into the intestines or peritoneal cavity. The contents of the abscesses were numerous shreds of partially disintegrated tissue, and a creamy, reddish-yellow fluid which much resembled pus. Under the microscope this fluid is found to consist of a mass of granular detritus, a few pus-cells, and numerous amœbæ. Pieces of the liver tissue were hardened and stained by the methods already described. In the edges of sections which had been taken from the walls of the abscesses and in small

abscesses, which could be examined entire, the pus-like fluid which they contained was found to consist largely of a granular mass, in which were a few pus-cells, some nearly destroyed liver-cells, here and there shreds of masses of fibrin, some fibrinous remains of the connective tissue of the liver, which often contained bloodvessels and bile-ducts, many amebic, and, at some points, multitudes of cocci. This fluid also contained numerous nuclei in a state of partial disintegration, and occasionally small masses of fat. (Fig. 4.) The most interesting of these constitu-

FIG. 4.



Section of edge of a liver abscess. Toluidin-blue and eosin. Beck 1 inch, Oc. 3. *a*, broken-down mass which constitutes the contents of the abscess; *b*, the abscess wall; *c*, the breaking down liver cells in the vicinity.

ents are the masses of connective tissues. They often lie at considerable distances from the abscess-wall, and frequently appear to have no connection with it. The degree of vitality which they show under these circumstances is certainly very remarkable. Around their edges the tissues are always softened, their nuclei are swollen, partially broken down, and do not take the stain, and all stages of disintegration may be observed. The central portions of these masses are comparatively little changed, but the tissues are somewhat cloudy and are swollen to a slight extent, and their nuclei are increased in number. Around the margins of these masses is a favorite haunt of the amebæ.

From the foregoing it will be at once seen that the contents of these abscesses is not pus—indeed, it much more closely resembles the cheesy

masses of tuberculosis. The walls of the abscesses differ somewhat, depending on their size and age. In the small and more recent ones it cannot be said that a wall exists, for the abscess contents gradually, and in a most irregular manner, merge imperceptibly into the surrounding half-degenerate liver-cells. In the larger abscesses the walls—while extremely irregular—are, as a rule, comparatively well defined, and consist of a mass of spindle-shaped or rounder bodies, which are evidently partially broken-down liver-cells. Frequently masses of fibrin constitute a part of the walls, and, interlacing between these cells, form a sort of reticulum. Amœbæ are often found along the inner border of the walls, and sometimes within them, but never penetrate farther than a few micromillimetres from the surface. Numerous colonies of bacilli resembling those found in the intestinal ulcers, and corresponding in their staining properties and their appearance to the colon bacilli, were found along the inner border within and beyond the walls. It would be difficult to conceive of a greater destruction of the liver-cells than occurs in the vicinity of the abscesses, and, indeed, most marked changes of the liver substance can be observed even at points most remote from these lesions. The liver-cells become granular, break up, and are detached from their capillaries. They also become much narrower than normal. Occurring usually in groups, are found very refractive granular cells, which evidently result from necrosis of the liver-cells. These bodies are almost always rounded or oval in shape, contain usually one or more well-defined nuclei, and generally many vacuoles, some of which are composed of fat, as may be seen in tissues fixed in osmic solutions. They are usually from eight to twenty micromillimetres in diameter, and might be easily mistaken for amœbæ. They are stained red with dark nuclei with the toluidin blue eosin method. Closely related to the above are very peculiar long, often irregular, somewhat spindle-shaped bodies, which take the place and result from the necrosis of liver-cells. Indeed, the tissue for some distance around the abscesses is composed almost entirely of these cells. They are highly refractive granular bodies, which contain vacuoles, and sometimes fat, and, occasionally, one is found containing a nucleus. They are from ten to fifty micromillimetres in length, and from three to ten in width. The peculiar variety of degeneration of the liver-cells just spoken of seems almost characteristic of this disease, as I have rarely seen it around abscesses which contained no amœbæ, and, at the most, I have seen only a few broken-down cells which somewhat resemble those found in the walls of amœbic abscesses. (Fig. 5.) Owing to the narrowing of the liver-cells the spaces between them are much increased in size, and within these spaces the capillaries are usually found detached from these cells. It often occurs that only traces of the capillary walls remain. Blood is conspicuously absent in the capillaries in the immediate vicinity of the abscesses, but,

in its stead, these vessels are often partially filled with the same kind of granular detritus that surrounds them. Occasionally, in the neighborhood of the abscesses, small areas are found in which the liver-tissue is almost entirely replaced by blood. This is evidently the result of hemorrhage from some of the larger vessels. The walls of the intralobular veins and those of such other vessels as are not surrounded by masses of fibrous tissue become infiltrated with cells as the necrotic process advances toward them, and later swell, soften, and break down. Not infrequently the bloodvessels were surrounded by a slight, small round-cell infiltration, but there is a remarkable absence of anything like a general inflamma-

FIG. 5.



Degenerating liver-cells and an amoeba. Toluidin blue and eosin. Beck $\times$, Oc. 3. Showing the various forms assumed by the degenerating liver-cells, and for the purpose of comparison an amoeba is represented in the lowest figure. The liver-cells are stained red with blue nuclei, while the amoeba is of an almost uniform dark-blue color.

tory reaction on the part of the tissues. In the tissues surrounding the abscesses, but never extending very deeply, numerous clumps of bacilli are seen, resembling in every way those found in the abscess-walls. The liver-cells, or the remnants of the same, which are in immediate contact with these bacilli are more completely broken down than the other cells in the vicinity, but this never extends to any distance.

It will be seen from the above, as pointed out by Councilman, that the soluble products of the amoebæ probably produce the extensive necrosis of the liver-tissue observed in the vicinity of the abscesses, but that complete breaking down and softening do not occur until the amoebæ come actually in contact with it.

The question as to how the amoebæ reach the liver has not as yet been

decided. Some have thought that they penetrated through the walls of the intestine, passed along the peritoneum, and burrowed their way through the capsule of the liver. This explanation seems to me extremely improbable. I think it all but certain that the amœbæ reached the liver by means of the portal circulation, as has been without doubt the case in instances recorded where there was a condition of almost miliary abscess of the liver. This view is also strengthened by the fact that the amœbæ are so frequently seen in the bloodvessels of the intestines.

Specimens of the kidneys were only examined in Cases XIV., XXII., and XXXV. In Cases XXII. and XXXV. the changes were limited to a slight granular degeneration of the lining-cells of the larger tubules, and there were very generally found collections of granular material, which stained faintly, in the spaces between the glomeruli and the capsule of Bowman. In Case XIV. the vessels were universally distended with blood. The cells of the tubules were intensely granular, their nuclei stained poorly or not at all, and they were frequently separated from their basement membrane and collected in masses in the centres of the lumina of the tubules. There was around the glomeruli none of the granular material described in connection with Cases XXII. and XXXV., but the nuclei of these bodies were considerably increased in number. There were no changes in the connective tissues of the kidneys, not even in the situations nearest to the liver-abscess.

There were no noticeable changes in the spleen.

After fixing specimens of the heart-muscle in Flemming's solution, many sections were made from Cases XIV. and XXII., for the purpose of determining as to whether fatty degeneration existed, but in neither was this found.

The lungs were normal in three of the four cases where autopsies were made. There were miliary tubercles in Case VI.

SYMPTOMS. The disease usually begins acutely, with slight fever, griping, tenesmus, and frequent stools. Occasionally, however, the onset is gradual, there being a period varying from a few days to several weeks, during which the stools, at first only somewhat watery and frequent, become gradually more dysenteric in character, and finally the symptoms in the two varieties merge insensibly into each other. If the acute form becomes severe, we find, with the exception that here the inflammatory phenomena are generally more marked, the same symptoms that occur in the severe chronic form. The disease, however, as we commonly meet with it, is pre-eminently a chronic one, and lasts all the way from a few weeks to many years. In this variety the general condition is often remarkably good, but in the severer forms great emaciation is frequently observed. Loss of appetite is common, but nausea and vomiting rarely occur. Fever and rapid pulse are decided only in the severer forms of

the affection. The patients complain of a sense of uneasiness in the abdominal region, with a more or less constant desire to go to stool, as the disease is of a severe or mild type. After the affection becomes chronic, tenesmus is, as a rule, slight; but during exacerbations it is often quite severe. For the purpose of convenience we may—somewhat arbitrarily, it must be confessed—divide, clinically, the chronic form of the disease into several types.

1. *The very mild form.* The appetite and general health are good; no fever or acceleration of the pulse worth mentioning. The number of stools varies from two to five or six in twenty-four hours. This is the usual form in children.

2. *The moderately severe form.* The general nutrition is here decidedly interfered with, and there is frequently more or less anorexia. The pulse is somewhat increased in frequency, and there are irregular exacerbations of temperature, occurring especially at night. The stools vary in number from six or eight to fifteen or twenty in twenty-four hours.

3. *The very severe form.* This differs but little from the severest of the acute type. There are great emaciation, loss of appetite, and sometimes nausea and vomiting. Profuse sweating may occur. Hiccough is frequent. The extremities are often cold, and the pulse is rapid and weak. The temperature varies much, but is usually somewhat above normal; as death draws near it sometimes becomes subnormal. The stools are watery, filled with blood, mucus, and sometimes sloughs, and vary from twenty to fifty in twenty-four hours. It is really wonderful how long patients will remain in this condition without dying, and in no disease may death be more closely approached and recovery follow.

There are remarkable fluctuations in the severity of the symptoms in all of the chronic forms, and especially does this apply to the number of stools. In the milder types there are often not more than three or four actions in twenty-four hours, but at any time the number may be increased to ten or fifteen, or even more. On the other hand, in the severest forms the number of stools may without any apparent cause suddenly decrease in number, which may continue until complete recovery results. It thus happens that we often see the mildest forms of this affection suddenly changing to the worst, and *vice versa*. It is a fact that some cases are greatly aggravated by the taking of alcoholics—beer seeming to be especially injurious. Any form of bodily exertion is generally followed by an exacerbation of the symptoms. A constant aching pain in the back, not relieved by the recumbent posture, is a symptom which has been prominent in several of my cases, and has caused a great deal of trouble. Pain, of a tearing character, in the region of the colon, is also an occasional symptom. Œdema of the feet and face is occasionally seen.

In the milder forms the urine is, as a rule, normal, but albumin was

noted in some of the severer cases, especially if the temperature was high. In some of my worst cases I have day after day carefully examined the urine for peptones, by Hofmeister's method, but never found them present. Chlorides may be much diminished or suppressed. Their reappearance or increase is a most favorable symptom.

The feces in the milder forms may appear almost normal in both color and consistency; but, on careful inspection, small particles of bloody mucus will be found lying here and there on their surfaces. In the most severe forms the stools are loose, and contain considerable quantities of mucus and blood, mixed with partially digested food, are very offensive, and, while the color varies considerably, a more or less reddish tinge is quite constant. The discharges in the worst forms of this affection are, I think, entirely characteristic. They consist of a soft, jelly-like mass which has an almost evenly distributed pink hue. Sometimes the amount of mucus is not so great, and, especially shortly preceding death, they may lose almost entirely their mucous character and become scarcely more than bloody water. They are almost always of an alkaline reaction. In two cases I have found the reaction slightly acid. On microscopical examination, the feces are found to consist of fragments of partially digested food, much mucus and blood, pus, large epithelioid cells, multitudes of bacteria, and varying numbers of amœbæ. *Cercomonas* are not infrequently found.

The most important complication of amœbic dysentery is hepatic abscess. Out of seventy-eight cases it occurred fifteen times, one of which was in a boy. This complication occurs only in the early stages, or, at the most, it is certainly very rare in the chronic cases. It would seem that it is more common in some localities than in others, for in my thirty-five cases it has occurred only twice. This is, I am sure, in a measure explained by the fact that the majority of my cases were seen only after the disease had become chronic. The usual symptoms are chills, fevers of an irregular character, acceleration of the pulse, and a throbbing or aching pain in the region of the liver, or the pain may be reflected to the right shoulder. At the same time the tongue becomes coated, the appetite fails, and the patient rapidly loses flesh. On physical examination, there is found enlargement of the liver, and occasionally a fulness or marked protrusion develops at the lower border of the ribs. Jaundice is rare. Sometimes the usual symptoms are absent, and, with the exception of a general cachexia, no symptoms exist.

If the liver-abscess opens into the lung, as it very frequently does, abscess of this organ develops. The symptoms are cough and the expectoration of reddish-brown fluid, which, on microscopic examination, is found to contain amœbæ. The usual signs of consolidation develop in the lung. This complication I have not seen; it has occurred only three times in seventy-eight cases.

When perforation of the intestine occurs and peritonitis follows, the symptoms which are usually produced under these circumstances follow. I do not think, however, that the inflammatory phenomena are ever so marked as in the septic peritonitis which follows operations.

Appendicitis would, of course, occasion the usual symptoms. However, in my case, which is, so far as I know, the only recorded one of the kind, the symptoms were of such a mild character that the condition was not suspected before death.

DIAGNOSIS. The diagnosis cannot be made with certainty except by finding the amœbæ. When we find, however, the patient suffering with a chronic dysentery that shows great variations in intensity, and which, moreover, resists all the usual remedies employed in the treatment of this affection, the probability becomes very strong that it is a case of amœbic dysentery, and should always lead to an immediate examination of the stools. Whether the amœbæ be the cause of this disease or not, I do not believe that it is possible to overestimate their value as a means of differentiating between this affection and conditions such as carcinoma and tuberculosis, for which it might be mistaken.

PROGNOSIS. This is a very fatal disease. Out of the seventy-eight cases reported in this country there have been thirty deaths. It usually occurs in a milder form in people of the colored race than in those of the white. It seems very certain that the disease is rarely so severe in children as in adults. After it becomes chronic, and in the vast proportion of cases it does become so, the chances of recovery, even with the best treatment, are always bad. However, at any time the disease may rapidly grow better, and the patient recover, or, on the other hand, it may become worse, and death result. After apparent recovery relapses frequently occur, and a patient should never be considered out of danger until many months after all traces of the disease have vanished. Spontaneous recovery sometimes occurs.

Liver-abscess is a very fatal complication, twelve out of the fifteen cases reported in this country having proved fatal.

Abscess of the lung is very grave, but it probably adds little to the existing danger, as an opening is thus made for the pus pent up in the liver-abscess.

Perforation of the intestine and peritonitis are probably always fatal. As mine is the only recorded case of amœbic appendicitis, and as this case was complicated by a liver-abscess, nothing can as yet be said respecting the prognosis, but it is doubtless very bad.

TREATMENT. As I have never happened to see a case of this variety of dysentery at the very beginning, I can say nothing from personal experience as to the treatment. It would, perhaps, be best to employ the remedies which are usually used in the common catarrhal forms of this affection. Ipecac especially deserves a thorough trial, as it is

the drug that has proved of the most benefit in the dysenteries of India, which are probably often amæbic in character. In the chronic form I have from time to time used almost everything which has ever been recommended in the treatment of this class of diseases, but have rarely seen any striking effect produced by them. In its behavior toward drugs this variety of dysentery is almost as capricious and variable as are its symptoms. Opium checks the number of discharges, but I have never seen any permanent good result from it. Sulphuric acid has in several cases apparently produced some benefit, but never a cure. One patient recovered while taking salol. The treatment heretofore most recommended has been rectal injections of 1:5000 aqueous solutions of quinine sulphate. I used this treatment with great persistence in some of my earlier cases, but not in a single instance was there the slightest perceptible result. Injections of 100:300 watery solution of bisulphate of quinine were somewhat beneficial in one or two instances. One patient recovered while using injections of potassium permanganate, but in several other cases no effect was observed. In not a single instance did improvement follow injections of ice-water. Several years ago, while speaking on this subject with my friend, Dr. I. B. Diamond, at that time a student, he suggested that, on account of its antiseptic effect, possibly hydrogen dioxide might be of service. With but little hope, I must confess, I tried it on Case V., with the result that the patient rapidly improved. As soon as she was strong enough to go to work she did so, and at the same time abandoned the treatment and resumed a solid diet. In a short time she relapsed, and was again treated in the same manner with a like result. She again stopped the treatment, and, although I have not since seen her, I learn that she again has the trouble. Since that time I have treated many of my patients with this agent, with the result that some have been cured, and, with but one or two exceptions, the improvement after its use has been striking and immediate. All hemorrhage at once ceases, the stools rapidly decrease in number, and the general condition grows better. The effect of this drug, however, is by no means constant—it benefiting some patients much more than others. Even in the same patient this sometimes holds good, for, in one or two instances, in relapses, after it had apparently effected a cure, its use a second time was wholly without benefit. The ordinary commercial hydrogen dioxide is diluted from four to eight times with water, and the solution injected. About a quart is injected twice daily, which, after a week, may be gradually decreased. This is the only agent which has in my hands proved of any decided value. I do not doubt that it would prove of equal value in all varieties of dysentery, especially in the chronic forms.

Hydrogen dioxide, as found in the market, is notoriously uncertain in strength, some samples being utterly valueless. If improperly prepared

it decomposes rapidly. This may, in a measure, explain the lack of uniformity in the results obtained by its use.

The diet should be liquid, whether the affection is acute or chronic. I have used milk almost entirely, and, as a change, occasionally egg-albumin.

The remarkable toxic effect of the toluidin blue on the amœbæ would suggest the employment of rectal injections of this substance in the treatment of the disease; but in the absence of any knowledge as to its action on the human being, I have not made the attempt.

My friend, Dr. E. A. Corson, of Savannah, Ga., some years ago suggested to me that in suitable cases the establishment of an artificial anus at the ileo-cæcal valve, and the subsequent washing out of the colon with hydrogen dioxide, might be employed with advantage.

In finally dismissing the subject I cannot forbear stating my conviction that imperfect hygienic conditions are indirectly responsible for the prevalence of amœbic dysentery, and that with even an ordinary attention to sanitary laws the disease would in a short time cease to exist.

I wish, in conclusion, to express my thanks to my friends, Mr. J. C. Haskell, Jr., for the drawings of the fixed amœbæ, and to Dr. I. B. Diamond for much valuable assistance.

TWO CASES OF CONGENITAL SYPHILITIC CIRRHOSIS OF THE LIVER IN INFANTS.

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THE following two cases, which came under my care within a short interval of each other, afford excellent examples of the changes in the liver in hereditary syphilis, in the one case more advanced than in the other, and leading to great destruction of the parenchyma of the organ :

The first patient was an infant of ten weeks; she was brought to the Bristol General Hospital with a history that she had appeared to be in pain in the stomach, that the belly had always been rather large, but that no distinct swelling had been observed until ten days previously, when a swelling in the upper part of the abdomen had appeared and had gradually increased.

During the same time the child had vomited all the milk she had taken. There had been no jaundice at any time, and no hemorrhage from the stomach or bowels; the child was fed at the breast; the bowels had been moved regularly, and the motions were normal. The urine was of normal appearance.

Both father and mother were healthy, according to the mother's statement, and had one other child, also healthy. The patient had suffered